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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|-----------------------|---------------------|------------------|
| 09/724,985 | 11/28/2000 | Philip Michael Savage | 674544-2001 | 8380 |

20999 7590 05/17/2006

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EXAMINER

VANDERVEGT, FRANCOIS P

ART UNIT PAPER NUMBER

1644

DATE MAILED: 05/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | | |
|------------------------------|------------------------|--|------------------------|--|
| Office Action Summary | Application No. | | Applicant(s) | |
| | 09/724,985 | | SAVAGE, PHILIP MICHAEL | |
| | Examiner | | Art Unit | |
| | F. Pierre VanderVegt | | 1644 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 November 2005 and 01 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,4,9,11-48 and 50-75 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4,9,11-14,16-18,26,27,29,32,33,37,46-48, 50-53,56,57,60,63,64,67-70 and 75 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims withdrawn from consideration are 15,19-25,28,30,31,34-36,38-45,54,55,58,59,61,62,65,66 and 71-74.

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DETAILED ACTION

This application is a continuation-in-part of Application Serial Number PCT/GB99/01764.

Claims 2, 5-8, 10 and 49 have been canceled.

Claims 1, 3, 4, 9, 11-48 and 50-75 are currently pending.

Claims 15, 19-25, 28, 30, 31, 34-36, 38-45, 54, 55, 58, 59, 61, 62, 65, 66 and 71-74 are withdrawn as being drawn to a non-elected invention.

Accordingly, **claims 1, 3, 4, 9, 11-14, 16-18, 26, 27, 29, 32, 33, 37, 46-48, 50-53, 56, 57, 60, 63, 64, 67-70 and 75 are the subject of examination in the present Office Action.**

Request for Interview

1. Applicant has requested that an interview with the Examiner and a Supervisory Examiner be held in the event that the response filed November 16, 2005 resulted in any Office Action being issued other than a Notice of Allowability.

However, in view of the NEW GROUNDS of rejection presented below, Applicant is being given an opportunity to review the new rejection prior to said interview being held. Accordingly, Applicant is invited to schedule said interview after having an opportunity to review the ground of rejection newly presented.

In view of further review of the language of the claims, the following ground of rejection has been modified. Due to reliance upon an interpretation not previously considered, the ground of rejection constitutes a NEW GROUND of rejection and this rejection is made NON-FINAL.

Applicant's remarks filed November 16, 2005 are addressed as they pertain to the present ground of rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

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The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. Claims 1, 3, 4, 9, 11-14, 16-18, 26, 27, 29, 32, 33, 37, 46-50, 52, 53, 56, 57, 60, 63, 64, 67-70 and 75 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,548,067 B1 to Seeman et al (filing date June 2, 1995; A on form PTO-892).

It was previously stated: "The '067 patent teaches a complex comprising an HLA class I molecule comprising a T cell binding portion and an attaching means for selectively attaching said HLA class I molecule to a target cell. The attachment means comprises a linking polypeptide with specific affinity for a molecule on the surface of the target cell, wherein the linking polypeptide is an antibody molecule that binds to an antigen on the target cell or a molecule that binds to a receptor on the cell (Figure 34, column 3, lines 11-24 and 49-62 in particular). The '067 patent teaches the binding of a recognition peptide (allodeterminant) to the HLA class I molecule (Fig. 1, column 1, lines 58-62 and column 9, lines 40-44 in particular). The '067 patent further teaches that the HLA class I molecule and the linking polypeptide of the complex are directly covalently linked to one another or that the complex comprises a coupling system forming a stable bridge between the HLA class I molecule and the linking polypeptide comprising the small molecules biotin and avidin (Abstract, Figure 34, column 3, lines 11-17 and column 4, lines 5-13 in particular). the '067 patent further teaches that the allotype of the HLA class I molecule of the complex may be different from the HLA class I haplotype of a subject the complex is administered to (column 3, line 38 to column 4, line 4 in particular). The prior art teaching anticipates the claimed invention.

Claims 29 and 75 are drawn to a pharmaceutical pack or kit and are included in this ground of rejection. The kit recited in the claims comprises three components, the claimed complex, wherein the complex is in one or more containers and written instructions for administering the complex to a patient. In regard to the containers, while the '063 does not explicitly recite the presence of a container, it would be readily appreciated by the artisan that the complex as taught by the '063 patent would have been held in a container. Accordingly, the '063 patent demonstrates possession of 2 of the 3 elements of the kit. However, the printed matter on the instructions does not lend patentable weight as a limitation of the claimed invention because the recited intended use does not physically or chemically change the nature of the agent within the container and the artisan can still use the agent for other purposes. The intended use of a product, in this case an HLA class I/attachment means complex, does not materially change the product as the product can still be used for other purposes, such as identifying and/or immobilizing target cells in vitro. The recited "limitations" only further limit the intended use method printed on the instructions and do not change the physical and/or chemical properties of the components of the kit. In *In re Haller* (73 USPQ 403 (CCPA 1947)) the Court decided upon a case in which "it is not alleged by the Examiner or the board that the use of the involved compound as an insecticide is old or obvious and, in fact a claim covering broadly a process comprising the application of that compound to insects for the purpose of destroying them, has been allowed. In the instant case the appealed claim calls for a packaged product of an old compound labeled to indicate that the compound is intended for use as an insecticide." It is respectfully submitted that the facts of *In re Haller* are directly pertinent to the instant case. Applicant relies, as in *In re Haller*, upon printed matter reciting an intended use of the otherwise old compounds and

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compositions. The Court noted in *In re Haller* that "It is well settled that the application of particular printed matter to an old article cannot render the article patentable" and decided that, "the mere labeling of an old composition as an insecticide does not make it a new or different composition within the meaning of the patent statutes" and "Whether the statement of intended use appears merely in the claim or in a label on the product is immaterial so far as the question of patentability is concerned" in affirming the rejection. In *In re Venezia* (189 USPQ 149 (CCPA 1976)) the Court decided that the kit components were limited by the instructions listed in the claims because said kit components had to be adapted in a particular manner in order to meet the final assembly instructions that were part of the claim. The Court stated however that, "what may or may not happen in the future is not a part of the claimed invention" (emphasis by Court). The Court decided that the instructions of the claim were material to the claim because, "Rather than being a mere direction of activities to take place in the future, this language imparts a structural limitation to the sleeve" (emphasis added). The court reasoned this position by stating, "this language also defines present structures or attributes of the part of the 'kit' identified as the housing, which limits the structure of the housing to those configurations which allow for the completed connector assembly desired." It is respectfully submitted that, in the instant case, the instructions do not modify the complex comprised in the claimed kit, i.e., the complex does not have to be altered for use commensurate with the instructions, rather the printed instructions merely set forth steps for what may be done with the kit components in the future. Accordingly, the printed instructions do not lend patentable weight to the claimed invention."

Applicant's arguments filed November 16, 2005 have been fully considered but they are not persuasive. Applicant argues that the '067 patent does not teach each and every element of the claimed invention because the '067 patent does not teach a recognition peptide bound to the MHC class I molecule. Applicant pointed out that the antigenic determinants referred to in the '067 patent are not separate peptides, but are domains of the MHC class I molecule itself. The Examiner concurs with this interpretation of the cited reference.

However, further review of the claimed invention shows that there is no requirement in the claim for the "recognition peptide" to actually be part of the complex. Claim 1 recites in lines 4-5 of the claim, "wherein the HLA class I molecule or fragment thereof binds or is attached to a recognition peptide." Accordingly, the claims require only that the HLA class I component of the complex is capable of binding to a recognition peptide, not necessarily bound to one. The '067 patent discloses in column 1 that one of the normal functions of HLA class I .alpha.1 and .alpha.2 domains is to assist in antigen presentation. The '067 patent is silent about whether a recognition peptide is bound by the HLA class I molecule, but, equally, there is no teaching or suggestion in the '067 patent that the HLA class I molecule of the complex is not capable of binding to a recognition peptide. Silence about a particular property does not necessarily constitute its absence. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that there is a difference between the materials, i.e., that the claims are directed to new materials and that such a difference would have been considered unexpected by one of ordinary skill in the art, that is, the claimed subject matter, if new, is unobvious. In the absence

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of evidence to the contrary, the burden is on the Applicant to prove that the claimed materials are different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989). Absent the presence of evidence to the contrary, it is reasonable to conclude that the HLA class I molecules taught by the '067 patent can "bind" to recognition peptides and therefore satisfy the metes and bounds of the claim.

It is respectfully submitted that amendment of the claim(s) to recite --is bound or attached to-- in place of "binds or is attached to" would overcome this ground of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 3, 4, 9, 11-14, 16-18, 26, 27, 29, 32, 33, 37, 46-49, 51-53, 56, 57, 60, 63, 64, 67-70 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,548,067 B1 to Seeman et al (filing date June 2, 1995; A on form PTO-892) in view of Neri et al (J. Invest. Dermatol. [1996] 107(2):164-170; U on form PTO-892).

It was previously stated: "The '067 patent has been discussed supra.

The '067 patent does not teach the use of calmodulin and calmodulin binding protein as paired small molecules for joining the HLA class I molecule of the complex to the attaching means of the complex.

Neri teaches a method and a compound for attaching an anti-tumor molecule to another active compound by recombinant production of a single chain version of the antibody with a calmodulin peptide

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attached to the C-terminus (see entire document). Neri teaches that therapeutic peptides can be attached to the antibody by attaching them to a high-affinity calmodulin ligand, such as calmodulin binding protein. It is noted that the 225.28S antibody taught by Neri is the same as one of the anti-tumor antibodies exemplified in the instant specification as a preferred embodiment of an attachment means.

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to replace the biotin - avidin/streptavidin taught by the '063 patent with the calmodulin - calmodulin binding protein taught by Neri. The artisan would have been motivated to make the substitution by the teaching of Neri that calmodulin is poorly immunogenic and can be targeted with chemically modified high-affinity calmodulin ligands (Abstract in particular). the artisan would have had a reasonable expectation of success based upon the teaching of Neri that calmodulin did not interfere with binding of antibody to target cells and that such an antibody construct is useful as a building block for therapeutic applications."

Applicant argues that Neri does not overcome the defects in the '067 patent. However, in view of the reinterpretation of the reference based upon the review of the claims, the applicability of the primary '067 patent reference has been changed. Accordingly, the rejection over the '067 patent in view of Neri remains unaltered without further comment.

The following NEW GROUND of rejection has been necessitated by Applicant's amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 is ambiguous and unclear in the recitation of "a linking polypeptide which binds r is attached." It is not clear what the element "r" represents in the structure of the complex. If this represents a typographical error, Applicant is invited to make the appropriate correction.

Conclusion

5. No claim is allowed.

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6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
June 7, 2005

PV

David A Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
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